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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,160	04/12/2005	Boris Y Shekunov	FER-14857.001.001	4722

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EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/531,160	SHEKUNOV ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/18/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/3/06, 4/20/06, 5/2 10 6*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Information Disclosure Statements filed on 5/3/06, 4/20/06, 5/2/06 and the Terminal Disclaimers of serial numbers 10/534,665, and 10/789,422 is acknowledged.

Status of Claims

Claims 1-21 are pending in the application.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-3, 5-10, 12-17, 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Subramaniam et al. US 5,874,029 (hereinafter "Subramaniam").

Subramaniam teaches a method and an apparatus useful for the production of microparticles and nanoparticles.

The steps are:

Adding a solvent to a solute forming a mixture.

Adding the mixture to the SCF (which is a non-solvent)

Getting the particles out of the solute. (see abstract)

The invention can be used in the pharmaceutical, food, chemical, electronics, catalyst, polymer, pesticide, explosives, and coating industries, all of which have a need for small-diameter particles (abstract). The method comprises solutes such as drug, polymer, and/or excipient materials are solubilized. The supercritical antisolvent used is

supercritical carbon dioxide (col. 6, lines 27, and 28), also a trifluoromethane is used (claim 12), which is encompassed by fluorocarbons recited in the current application, and poly-lactide glycolide copolymers (claim 22).

Subramaniam discloses the limitation recited in claim 8 regarding functional group of portion that is SCF-philic and SCF-phobic since the current specification discloses in paragraph [0015 and 0027] teaches that any compounds that comprise both SCF-philic groups, which make the compound soluble in SCF, and SCF-phobic groups, which have an affinity or attraction to the nuclei of the material(s) formed during the precipitation step, can be employed as growth retardant compounds. Examples of growth retardant compounds for use with supercritical carbon dioxide (SC--CO_2) include fluorocarbons. Accordingly, Subramaniam discloses a trifluoromethane, which is encompassed by the group of fluorocarbons. In addition the limitation recited in independent claim 15 of the instant application regarding expanding the SCF solution across a pressure drop below the critical pressure of the SCF whereby the SCF decompresses and causes supersaturation and nucleation of particles comprising the solute material, said particles having a smaller size and a reduced amount of agglomeration than if no growth retardant compound was present. Subramaniam discloses that following the drying period, the pressure is decreased to atmospheric level (col. 9, lines 11-24). Furthermore Subramaniam teaches that accurate pressure control is essential in the highly compressible near-critical region. Pressure fluctuations in this region have a strong effect on the level of expansion of the organic solution and

thus on the level of supersaturation and nucleation (col. 9, 25-29, col. 5, line 40, 41 and example 1).

Conclusion: claims 1-3, 5-10, 12-17, 19-21 are anticipated by Subramaniam.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Subramaniam et al. US 5,874,029 in view of Tarara et al US 20030064029 (hereinafter "Tarara").

Subramaniam has been discussed above.

Subramaniam is deficient in disclosing growth retardant as sugar acetate, fluorocarbons or block polymers.

Tarara discloses engineered particles that may be used for the delivery of a bioactive agent to the respiratory tract of a patient. Tarara produces the particulates under supercritical conditions [0088]. The patent discloses the use of block copolymers [0056], polymer resins of ethylene-vinyl acetate, ethylene-acrylic acid [0063], polycationic materials such as polyacrylic acid [0066], and polyethylene glycol [0057].

Accordingly, it would have obvious to a skilled man in the art to expand the teachings of Subramaniam and add the block polymers recited by Tarara since Tarara is producing fine particles for respiratory tract use, it would make a good motivation to the artisan to combine and produce a particulate drug using supercritical fluid to obtain pharmaceutical particles for use in the respiratory tract.

Response to Arguments

3. Applicant's arguments filed 4/18/06 have been fully considered but they are not persuasive.

Rejection under USC 35 § 102

Applicant argues that Subramaniam teaches a solution comprising a solvent and a solute is sprayed out of a nozzle in the form of atomized droplets into a supercritical antisolvent, which causes depletion of the solvent in the atomized droplets and recrystallization of the solute in the form of particles. The difference between the process according to Subramaniam et al. and conventional supercritical anti-solvent

processes is that Subramaniam et al. teaches that the solution should be introduced into the nozzle together with an "energizing gas" (which Subramaniam et al. also refers to as a "compressed fluid" or "compressed gas (see col. 8, lines 9- 10) that exits the nozzle at a velocity such that the spray of solution is "shattered into extremely small droplets at the nozzle exit" (col. 6, lines 1-8). Subramaniam et al. teaches that "contact between the extremely small spray droplets and a turbulent stream of virtually pure antisolvent results in high solvent depletion rates, i.e. high mass transfer rates, and low probability for droplet coalescence" (col. 6, lines 13-18).

To respond to these arguments, examiner asserts that In the GAS process, a solute of interest (typically a drug, polymer or both) that is in solution or is dissolved in a conventional solvent to form a solution is sprayed, typically through conventional spray nozzles, such as an orifice or capillary tube, into supercritical CO.sub.2 which diffuses into the spray droplets causing expansion of the solvent. Because the CO.sub.2 - expanded solvent has a lower solubilizing capacity than pure solvent, the mixture can become highly supersaturated and the solute is forced to precipitate or crystallize (col. 3, lines 62+), the disclosure shows that it is not a must to use a gas energizer for spraying the droplest.

In contrast to the method and apparatus according to Subramaniam et al., the invention as claimed in the present application requires that a growth retardant compound that is at least partially soluble in the SCF and includes at least one functional group or portion that is ScF-philic and at least one functional group or portion that is ScFlphobic or solute material-philic to be:

(1) present in the solution that is sprayed into the SCF, as claimed in claims 1- 7., or

(2) dissolved in the SCF into which the solution is sprayed, as claimed in claims 8-14., or

(3) dissolved in the SCF together with a solute that is sprayed across the pressure drop, as claimed in claims 15-21.

The growth retardant compound protects or shields the developing particle nuclei precipitated upon depletion of the solvent thereby preventing the particles from agglomerating into larger particles. Applicants' mechanism for obtaining small particles is thus a chemical mechanism as opposed to a physical mechanism such as used in Subramaniam et al.

To respond to these arguments, examiner showed in the previous office action that "Subramaniam discloses that functional group of portion that is SCF-philic and SCF-phobic since the current specification discloses in paragraph [0015 and 0027] teaches that any compounds that comprise both SCF-philic groups, which make the compound soluble in SCF, and SCF-phobic groups, which have an affinity or attraction to the nuclei of the material(s) formed during the precipitation step, can be employed as growth retardant compounds. Examples of growth retardant compounds for use with supercritical carbon dioxide (SC--CO_2) include fluorocarbons." (See office action page 3)

Applicant also argues that Subramaniam et al. does mention trifluoromethane (which is a "fluorocarbon"), but only in the context of trifluoromethane being used as a supercritical anti-solvent. Subramaniam et al. does not teach the use of trifluoromethan

or any other fluorocarbon as a growth retardant compound present in a solution that is sprayed into a SCF, as claimed in claims 1-7., as a growth retardant compound dissolved in a SCF into which a solution is sprayed, as claimed in claims 8-14., or as a growth retardant compound that is dissolved in a SCF together with a solute that is sprayed across a pressure drop, as claimed in claims 15-21. Clearly, the process according to Subramaniam et al. is substantially difierent than the process claimed in the present application. The rejection of claims 1-3, 5- 10, 12-17 and 19-21 under 35 U.S.C. j102(b) as being anticipated by Subramaniam et al. is clearly improper. Reconsideration is respectfully requested.

A compound and its properties are not separable; the prior art clearly includes a fluorocarbon in a similar process. It is not necessarily that the prior art recognizes each and every advantage that a compound can accrue from the use of the particular compound. It is expected that the compound will achieve the retardant purpose intended by the instant application.

Rejection under USC 35 § 103

Applicant argues that Tarara et al. cannot be relied upon to overcome the deficiencies in the teachings of Subramaniam et al. as applied to the present claims. Tarara et al. is directed to the formation of "perforated microstructures" that can be used for inhaled drug therapy. The "perforated microstructures" according to Tarara et al. are formed via a spray drying process that employs a "blowing agent" and uses "commercially available equipment" (paragraph (00251).

In response to the previous argument, Tarara discloses that "the perforated microstructure powders may be dispersed in an appropriate suspension medium to provide stabilized dispersions for delivery of a selected agent. Such dispersions are particularly useful in metered dose inhalers and nebulizers. In this regard, particularly preferred suspension mediums comprise fluorochemicals (e.g. perfluorocarbons or fluorocarbons) that are liquid at room temperature" [0033].
This proves that at the time the instant invention was made it was clear for a skilled man in the art to use these compounds as retardants.

Tarara et al. teaches that in some applications it is desirable to retain high amounts of the "blowing agent" in the spray-dried product (see paragraphs (0087) and (00881). In order to retain the "blowing agent" in the "perforated microstructures", Tarara et al. teaches that the outlet temperature of the spray drying device should be about 20OC to about 150OC below the boiling point of the "blowing agent" (see paragraph (00881). It is in this context that Tarara et al. mentions that "In some cases, the temperature differential can be outside this range such as, for example, when producing the particulates under supercritical conditions or using lyophilization techniques" (paragraph (00881). This is the only instance in Tarara et al. where the word "supercritical" is mentioned. It is inconceivable how one of ordinary skill in the art, in view of Tarara et al. taken as a whole, would be motivated to modify the process according to Subramaniam et al. to incorporate a growth retardant compound such that it is: (1) present in the solution that is sprayed into the SCF, as claimed in claims 1- 7., or

(2) dissolved in the SCF into which the solution is sprayed, as claimed in claims 8-14, or (3) dissolved in the SCF together with a solute that is sprayed across the pressure drop, as claimed in claims 15-21.

To respond to these arguments, the examiner would like to call the attention of the Applicant to the office action page 4 bridging to page 5, where it is cited that Tarara recognized the fact that producing the particulates under supercritical conditions using block copolymers, polymer resins of ethylene-vinyl acetate, ethylene-acrylic acid improves the blowing agent. Furthermore, Subramaniam disclosed the same steps of the current method including adding a solvent to a solute forming a mixture, adding the mixture to the SCF (which is a non-solvent), and getting the particles out of the solute. (see abstract). Applicants indicate improved chemical of preventing the agglomeration into larger particles (remarks page 8) over prior art teachings however the degree of improvement is not reflected in the claim by reference points, which could be used to compare with the prior art.

In addition, it is expected that a skilled artisan would be motivated to combine subramaniam and Tarara because Tarara explains further the use of the block copolymers and its effect on improving blowing a biological agent from a nozzle.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

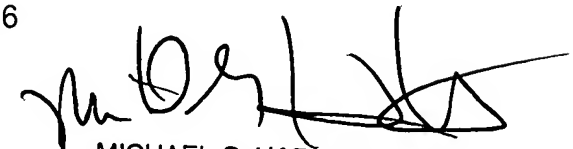
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim

6/23/06



MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER